THE MERCK INDEX

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CHEMICALS, DRUGS, AND BIOLOGICALS

TWELFTH EDITION

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of neuromuscular blockade: D. *iology* **61**, 428 (1984). Clinical schycardia: J. Frieden *et al., Am.* J. D. Cantwell *et al., Arch. Int.* gnostic use in myasthenia gravis: *in. Exp Neurol.* **19**, 45 (1983); I. **2**, 1 (1986); in esophageal chest *Ann. Int. Med.* **103**, 14 (1985); C. **32**, 682 (1987).

ol, dec 162-163°. pH of 1% aq r; freely sol in alcohol. Insol in

edrophone bromide, Ro-2-3198. ther, dec 151-152°. Bitter taste. (0%). Moderately sol in alcohol. Solns are stable.
c antidote to curare principles. gravis; esophageal chest pain).

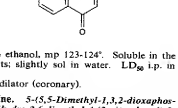
xy-1(2H)-quinolinecarboxylic acid -ethoxy-1,2-dihydroquinoline; *N*-1,2-dihydroquinoline; BC-681. C 68.06%, H 6.93%, N 5.66%, used in the synthesis of peptides: *m. Soc.* **90**, 1651 (1968); Yajima, *Bull.* **19**, 1905 (1971); Sipos, Gas- reparation: Weinberg, U.S. pats. (1968, 1969, to Bristol-Myers). ity: Belleau, *J. Am. Chem. Soc.* ological studies: Martel *et al.*, L. **47**, 909 (1969); Chang *et al.*, **2**, 63 (1970); Weissman, Muren, 1).

l'.
peptides.

(Difluoromethyl)-DL-ornithine; *α*-)FMO; RMI-71782. $C_6H_{12}F_2$ 39.56%, H 6.64%, F 20.86%. Si rsible inhibitor of ornithine de- Metcalf *et al., J. Am. Chem. Soc. et al., J. Org. Chem.* **44**, 2732 fects on cultured tumor cells: P. *Biophys. Res. Commun.* **81**, 58 ells in rats: L. Alhonen-Hongis- **B33**, 559 (1979). Inhibition of Hölttä *et al., Biochem. J.* **178**, mal activity in mice: C. J. Bac- 2 (1980). Pharmacokinetics in *l al., Clin. Pharmacol. Ther.* **30**, uations in *Pneumocystis carinii et al., West. J. Med.* **141**, 613 S. Van Nieuwenhove *et al.*, *t. Hyg.* **79**, 692 (1985); in cancer off *et al., Cancer Treat. Rep.* **70**, al., *ibid.* **71**, 459 (1987).

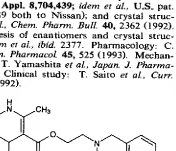
Hydrochloride monohydrate, $C_6H_{13}F_2N_3O_2 \cdot HCl \cdot H_2O$. ***Ornidyl.*** Crystals from ethanol/water, mp 183°.
THERAP CAT: Antineoplastic; antipneumocystis; antiprotozoal (Trypanosoma).

3565. Efloxate. *[4-Oxo-2-phenyl-4H-1-benzopyran-7-yl)oxy]acetic acid ethyl ester;* 7-flavone ethyl hydroxyacetate; ethyl flavon-7-yloxyacetate; ethyl 7-flavonoxyacetate; 7-flawonoxyacetic acid ethyl ester; oxyflavil; Re-1-0185; Reecordil. $C_{19}H_{16}O_5$; mol wt 324.33. C 70.36%, H 4.97%, O 24.67%. Prepn: Colleoni, Setnikar, *Farmaco Ed. Sci.* **13**, 561 (1958); **Brit. pats. 803,372, 824,547** (1958, 1959 to Recordati); Da Re, Colleoni, *Ann. Chim. (Rome)* **49**, 1632 (1959).



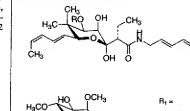
Crystals from 50% ethanol, mp 123-124°. Soluble in the usual organic solvents; slightly sol in water. LD_{50} i.p. in rats: 3200 mg/kg.
THERAP CAT: Vasodilator (coronary).

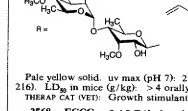
3566. Efonidipine. *5-(5,5-Dimethyl-1,3,2-dioxaphosphorinan-2-yl)-1,4-dihydro-2,6-dimethyl-4-(3-nitrophenyl)-3-pyridinecarboxylic acid 2-[phenyl(phenylmethyl)amino]ethyl ester, P-oxide;* 2-(*N*-benzylanilino)ethyl(±)-1,4-dihydro-2,6-dimethyl-4-(*m*-nitrophenyl)-5-phosphononicotinate, cyclic 2,2-dimethyltrimethylene ester. $C_{34}H_{36}N_3O_7P$; mol wt 631.67. C 64.65%, H 6.06%, N 6.65%, O 17.73%, P 4.90%. Dihydropyridine calcium channel blocker. Prepn: K. Seto *et al.*, **PCT Int. pat. Appl. 8,704,439;** *idem et al.*, **U.S. pat. 4,885,284** (1987, 1989 both to Nissan); and crystal structure: R. Sakoda *et al., Chem. Pharm. Bull.* **40**, 2362 (1992). Stereoselective synthesis of enantiomers and crystal structure of (*S*)-form: *idem et al., ibid.* 2377. Pharmacology: C. Shindo *et al., J. Pharm. Pharmacol.* **45**, 525 (1993). Mechanism of action study: T. Yamashita *et al., Japan. J. Pharmacol.* **57**, 337 (1991). Clinical study: T. Saito *et al., Curr. Ther. Res.* **52**, 113 (1992).



Crystals from ethyl acetate, mp 169-170° (Sakoda); also reported as mp 155-156° (Seto).
Hydrochloride, $C_{34}H_{36}N_3O_7P \cdot HCl$. LD_{50} in mice (mg/kg): > 600 orally (Seto).
Hydrochloride ethanol, $C_{34}H_{36}N_3O_7P \cdot C_2H_5OH \cdot HCl$, *NZ-105, Landel.* Yellow crystals from aq ethanol, mp 151° (dec).
(*S*)- or (*R*)-Form, pale yellow crystals from ethanol, mp 190-192°. $[\alpha]_D^{25}$ + or −7.0° resp (c = 0.50 in chloroform).
THERAP CAT: Antihypertensive.

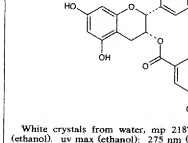
3567. Etrotomycin. *31-O-[6-Deoxy-4-O-(6-deoxy-2,4-di-O-methyl-α-mannopyranosyl)-3-O-methyl-β-D-allopyranosyl]-1-methylmocimycin; 31-O-[6-deoxy-4-O-(6-deoxy-2,4-di-O-methylhexopyranosyl)-3-O-methylhexopyranosyl]-1-methylmocimycin;* FR-02A; MK-621; Produci. $C_{68}H_{98}N_2O_{26}$; mol wt 1445.35. C 61.87%, H 7.74%, N 2.45%, O 27.94%. Antibiotic produced by *Streptomyces lactamdurans* NRRL 3802: R. G. Wax, W. M. Maiese, Ger. pat. **2,450,813** (1975 to Merck & Co.); *C.A.* **83**, 145755y (1975); R. G. Wax *et al., J. Antibiot.* **29**, 670 (1976). *In vitro* and *in vivo* activity: B. M. Frost *et al., ibid.* 1083; **32**, 626 (1979). Production and growth promoting activity: W. M. Maiese, R. G. Wax, U.S. pat. **4,024,251** (1977 to Merck & Co.). Synergism with bottromycin, q.v.: B. M. Frost *et al., J. Antibiot.* **32**, 1046 (1979). Structure: R. S. Dewey *et al., ibid.* **38**, 1691 (1985). Stereospecific total synthesis: R. E. Dolle, K. C. Nicolaou, *J. Am. Chem. Soc.* **107**, 1691, 1695 (1985). HPLC determn in feeds: J. D. Rosen, *Analyst* **111**, 853 (1986). Effect on gain and feed efficiency in swine: A. G. Foster *et al., J. Anim. Sci.* **65**, 877 (1987).





Pale yellow solid. uv max (pH ?): 232, 327 nm ($E_{1cm}^{1\%}$ 464, 216). LD_{50} in mice (g/kg): > 4 orally; > 2 s.c. (Frost).
THERAP CAT (VET): Growth stimulant.

3568. EGCG. *3,4,5-Trihydroxybenzoic acid, (2R-cis)-3,4-dihydro-5,7-dihydroxy-2-(3,4,5-trihydroxyphenyl)-2H-1-benzopyran-3-yl ester;* (−)-epigallocatechin 3-*O*-gallate; (−)-epigallocatechol gallate. $C_{22}H_{18}O_{11}$; mol wt 458.38. C 57.65%, H 3.96%, O 38.39%. Polyphenolic constituent of tea; inhibits tumor promotion. Initial identification and isoln from green tea: M. Tsujimura, *Bull. Agr. Chem. Soc. Japan.* **6**, 70 (1930); *C.A.* **25**, 3637 (1931); and crystallization: L. Yuataz *et al., J. Chromatog.* **2**, 173 (1959). Oxidation during tea fermentation: P. Coggon *et al., J. Agr. Food Chem.* **21**, 727 (1973). HPLC/MS extraction from black tea: R. G. Bailey *et al., J. Sci. Food Agric.* **66**, 203 (1994). HPLC determn in plasma and urine: M.-J. Lee *et al., Cancer Epidemiol. Biomark. Prev.* **4**, 393 (1995). Antitumor promoting activity: S. Yoshizawa *et al., Phytother. Res* **1**, 44 (1987); T. Yamane *et al., Cancer Res.* **55**, 2081 (1995). Inhibition of metastasis in mice: S. Taniguchi *et al., Cancer Letters* **65**, 51 (1992). Brief review of early work: E. A. H. Roberts, *J. Sci Food Agric.* **3**, 193-198 (1952).



White crystals from water, mp 218°. $[\alpha]_D$ −185° ±2° (ethanol). uv max (ethanol): 275 nm (ε 11500).

3569. EGF-Urogastrone. EGF-URO. Related polypeptides that are both potent stimulators of cellular proliferation and inhibitors of gastric acid secretion. *Urogastrone* was originally detected as an antisecretory agent during experiments on human urine: J. S. Gray *et al., Science* **89**, 489 (1939); M. H. F. Friedman *et al., Proc. Soc. Exp. Biol. Med.* **41**, 509 (1935). Isoln: J. S. Gray *et al., Endocrinol.* **30**, 129 (1942); R. A. Gregory, *J. Physiol.* **129**, 528 (1955). Improved procedures led to the isoln and amino acid sequence determn of two polypeptides, *β-urogastrone* and *γ-urogas-*